REMARKS

Applicant respectfully requests reconsideration. Claims 1-3, 7-17, 139, 142, 144, 166, 251-260, 338 and 340-348 were previously pending in this application. By this amendment, Applicant is canceling claim 340 without prejudice or disclaimer. Claim 1 and 341 have been amended. Claim 1 has been amended to advance prosecution and to clarify claim language. Support for the amendment to claim 1 can be found in the specification on page 59, lines 23-32. Claim 341 has been amended to correct claim dependency in view of the cancellation of claim 340. As a result, claims 1-3, 7-17, 139, 142, 144, 166, 251-260, 338 and 341-348 are pending for examination with claim 1 being an independent claim.

No new matter has been added.

Rejections Under 35 U.S.C. §103

Claims 1-3, 8-17, 139, 144, 166, 251-260, 338 and 340-347 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,090,365), as evidenced by Ajay et al. (Proc. Am. Soc. Clin. Oncol. 2001; 20: Abstr 1118) in view of Wallner et al. (WO 00/71135).

Without conceding the correctness of the Examiner's position and in order to advance prosecution, Applicant amended independent claim 1. As currently amended, claim 1 (from which all the rejected claims depend) is directed to a method for enhancing treatment with an anti-CD20 antibody (such as rituximab) or a fragment thereof in a subject having a cancer that is *refractory to rituximab* by combining the anti-CD20 antibody with an agent of Formula I (such as Val-boroPro).

An obviousness rejection based on a combination of references requires that the combination of the references must result in each and every limitation of the rejected claims, a motivation or suggestion to combine the cited references, and a reasonable expectation of success relating to such a combination.

The combination of the cited references does not teach or suggest the elements of the instant claims as currently amended namely, that treatment with an anti-CD20 antibody (such as rituximab) is enhanced by an agent of Formula I (such as Val-boroPro) in a subject having a cancer that is

refractory to rituximab. The instant specification documents this enhanced response in a mouse model of Burkitt's Non-Hodgkin's lymphoma in Fig. 3 and Example 4. In this model, when the anti-CD20 antibody rituximab was administered in conjunction with the Formula I agent, Val-boroPro (i.e., PT-100), tumor growth was inhibited to a significantly greater extent than occurred with the antibody alone.

Also, Applicant previously submitted a Declaration under 37 CFR 1.132 by Margaret Uprichard describing the unexpected findings relating to the combined use of an agent of Val-boroPro and rituximab. As stated in the Uprichard Declaration, similar results have been observed during Phase II clinical trials using rituximab and Val-boroPro. These results were presented at the American Society of Hematology Annual Meeting in December 2005. These data show that anti-cancer responses can be achieved using rituximab and Val-boroPro in patients who failed a prior rituximab regimen. These trials were conducted in accordance with methods described in the instant patent application. The results demonstrate that the therapeutic effect of the anti-CD20 antibody can be enhanced by using the antibody in conjunction with a Formula I agent in a subject having a cancer that is refractory to rituximab, and, thus, they further support the invention as described in this instant application and as claimed.

Furthermore, the teachings of the cited prior art do not provide the motivation, let alone a reasonable expectation of success, for one of ordinary skill in the art to use an anti-CD20 antibody (such as rituximab) to enhance treatment with the anti-CD20 antibody in a subject having a cancer that is *refractory to the anti-CD20 antibody rituximab*. In other words, based on the teachings of the of the prior, one of ordinary skill in the art would not be motivated to administer an anti-CD20 antibody (such as rituximab) to a subject that has a cancer that is not responsive to rituximab and would not have a reasonable expectation of success by doing so because the subject will not be expected to respond to treatment with an anti-CD20 antibody (such as rituximab).

Thus, the instant claims are patentable under 35 U.S.C. 103 over Kaminski et al., in view of Ajay et al. and in view of Wallner et al. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 1-3, 7-17, 139, 144, 251-260, 338 and 348 are rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson et al. (U.S. Patent No. 5,776,456) as evidenced by Grillo-Lopez et al. (Current Pharmaceutical Biotechnology, 2000, 1:1-9) in view of WO 00/71135 to Wallner et al.

Without conceding the correctness of the Examiner's position and in order to advance prosecution, Applicant amended independent claim 1. As currently amended, claim 1 is directed to a method for enhancing treatment with an anti-CD20 antibody (such as rituximab) or a fragment thereof in a subject having a cancer that is *refractory to rituximab* by combining the anti-CD20 antibody with an agent of Formula I (such as Val-boroPro). The arguments presented above in response to the rejection of the claims as obvious over Kaminski et al., in view of Ajay et al. and in view of Wallner et al. are reiterated and are applicable here. The combination of the Anderson et al., Grillo-Lopez et al., and Wallner et al. references does not teach or suggest the elements of the instant claims as currently amended, particularly that treatment with an anti-CD20 antibody (such as rituximab) is enhanced by an agent of Formula I (such as Val-boroPro) in a subject having a cancer that is *refractory to rituximab*.

Furthermore, the teachings of the cited prior art do not provide the motivation, let alone a reasonable expectation of success, for one of ordinary skill in the art to use an anti-CD20 antibody (such as rituximab) to enhance treatment with the anti-CD20 antibody in a subject having a cancer that is *refractory to the anti-CD20 antibody rituximab* for the reasons stated above.

Thus, the instant claims are patentable under 35 U.S.C. 103 over Anderson et al., in view of Grillo-Lopez et al., and in view of Wallner et al. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 340-347 are rejected under 35 U.S.C. §103(a) as being unpatentable over Anderson et al. (U.S. Patent No. 5,776,456) as evidenced by Grillo-Lopez et al. (Current Pharmaceutical Biotechnology, 2000, 1:1-9) in view of Wallner et al. (WO 00/71135), and further in view of Grillo-Lopez et al. (Current Pharmaceutical Biotechnology, 2000, 1:1-9).

Claim 340 has been cancelled. Claims 341-347 depend from claim 1. As currently amended, claim 1 is not obvious over Anderson et al., Grillo-Lopez et al., and Wallner et al. because the combination of the cited references does not teach or suggest the elements of currently amended claim 1 and claims 341-347 that depend from claim 1.

Additionally, the cited references alone or in combination, and for the reasons recited above, do not provide the motivation, let alone the reasonable expectation of success, for one of ordinary skill in the art to treat a subject having a cancer that is *refractory to rituximab* with an anti-CD20 antibody (such as rituximab).

Thus, the instant claims are patentable under 35 U.S.C. 103 over Anderson et al. as evidenced by Grillo-Lopez et al. in view of Wallner et al., and further in view of Grillo-Lopez et al. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim 142 is rejected under 35 U.S.C. §103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,090,365), as evidenced by Gopal et al. (Proc. Am. Soc. Clin. Oncol., 2001) in view of Wallner et al. (WO 00/71135) , and in further view of Buske et al. (European J. of Cancer, 1999).

Claims 142 depends from claim 1. As currently amended, claim 1 is not obvious over Kaminski et al. as evidenced by Gopal et al. in view of Wallner et al. and in further view of Buske et al. because the combination of the cited references does not teach or suggest the elements of currently amended claim 1 and claim 142 that depends from claim 1. Reconsideration and withdrawal of this rejection is respectfully requested.

In view of the claim amendments and above arguments, withdrawal of the rejection of the claims under U.S.C. 103 is kindly requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

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Respectfully submitted,

By _____

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